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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF	:
MAKOTO ONO, ET AL.	: EXAMINER: LOEWE
SERIAL NO: 10/562,122	:
FILED: DECEMBER 23, 2005	: GROUP ART UNIT: 1626
FOR: CYCLOHEXANECARBOXYLIC ACID COMPOUND	:

DECLARATION UNDER 37 C.F.R. §1.132

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

I, the undersigned, Makoto Ono, state that:

1. I am a graduate of Tokyo University of Science, Tokyo, Japan and received a master's degree in pharmaceutical science in 1989. I also received a PhD degree in pharmaceutical science in 2002 from Chiba University, Chiba, Japan.

2. I have been employed by Daiichi Pharmaceutical Co., Ltd. (as from April 2007, DAIICHI SANKYO Co., Ltd.) since April 1989, and since April 1992, I have been a researcher on physicochemical properties of drug, especially physical properties of crystals.

3. I understand the English language or, at least, that the contents of the Declaration were made clear to me prior to executing the same.

4. I am familiar with the above-identified application and know that the current claims, define specific crystals of sodium trans-4-[1-[2,5-dichloro-4-[(1-methyl-1H-3-indolylcarbonyl)amino]phenylacetyl]-(4S)-methoxy(2S)-

pyrrolidinylmethoxy]cyclohexanecarboxylate pentahydrate and medicinal compositions containing this that are in the form of a tablet, powder, granule, and capsule.

5. I understand that the U.S. Patent Office has rejected the medicinal composition claims of this application as being not capable of being made and/or used based on what is described in a publication to Brittain et al #2 "Effects of pharmaceutical processing on drug polymorphs and solvates" in Polymorphism in Pharmaceutical solids, vol. 95, p331-361.

6. I have read and understand what is described by Brittain but disagree that this publication applies to the medicinal composition claims as noted above.

7. The significance of the present invention lies in the technological accomplishment that is the first success in isolating the crystal form of a sodium cyclohexanecarboxylate pentahydrate as described in this application. It has been found that this crystallized compound exhibits higher water-solubility and causes no substantial weight change despite moisture adsorption/desorption, and is excellent in long term storage stability (see [0005], Table 3 and FIG. 5 of the application).

8. Moreover, the crystallized compound has the ability to maintain its crystallization continuously even when contained in a pharmaceutical preparation (e.g. capsule). Therefore, it is possible for a solid-type medicine to significantly improve in long term storage stability when containing such a crystal form of the compound.

9. An additional experiment has been performed demonstrating that the crystallized compounds as provided for in the claims of this application are capable of maintaining crystallization effectively as a component in a capsule.

10. Pattern (a) in the attached Fig. 6 shows the powder X-ray diffractometry spectrum of the Type-II crystallized compound as provided in the claims. Pattern (b) in Fig. 6 shows the powder X-ray diffractometry spectrum of a capsule comprising the Type-II crystallized compound of the present invention and an additive agent. Pattern (c) in Fig. 6 shows the

powder X-ray diffractometry spectrum of a capsule comprising a lactose monohydrate (which was used instead of the Type-II crystallized compound of the present invention) and an additive agent. The additive agent used in Pattern (b) is the same as that of the additive agent used in Pattern (c) with regard to their formulation and quantities.

11 The peak characteristic of the Type-II crystallized compound as provided in the claims has been found to become almost invisible at the region where the peaks derived from the additive agent make crossover, especially around 20°. In contrast, the other peaks characteristic of the Type-II crystallized compound have been clearly observed at the regions where there is no or little crossover of the peaks derived from the additive agent (e.g. 7.2°, 14.4°, 14.8°, 17.3° and 20.4°). From these data, it is evident that the Type-II crystallized compound is significantly capable of maintaining the continued crystallization as a medicine, among others.

12. Therefore, in my view formulating a crystalline compound as defined in the claims of the application into a medicinal composition that is the form of a tablet, powder, granule, and capsule would not have the issues that are identified in the Brittain publication cited by the U.S. patent office.

13. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Makoto Ono
Signature

January 13, 2009
Date